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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/809,790	03/26/2004	Maurice Zauderer	1843.0120001/AJK	7155

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STERNE, KESSLER, GOLDSTEIN & FOX PLLC
1100 NEW YORK AVENUE, N.W.
WASHINGTON, DC 20005

EXAMINER	
DIBRINO, MARIANNE NMN	
ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 06/02/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/809,790	ZAUDERER ET AL.	
	Examiner	Art Unit	
	DiBrino Marianne	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *3/26/04 & 3/14/05*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-60* is/are pending in the application.

4a) Of the above claim(s) *6-8,10-15,17,18 and 20-60* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,9,16 and 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/27/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant is required under 37 C.F.R. 1.821(d) to amend the specification to list the appropriate SEQ ID NO for sequences disclosed in the specification (for example, page 70 at [0205], line 3 and on page 71 at [0206], line 3, both for the nucleic acid sequence GTAAGT).

2. Applicant's amendment filed 3/26/04 and Applicant's response filed 3/14/05 are acknowledged and have been entered.

3. Applicant's election with traverse of Group I (claims 1-19), and species of cell surface markers from tumor cells and species of antigenic peptide derived from an infectious agent/infected cell in Applicant's said response filed 3/14/05 is acknowledged.

The basis for the traversal is of record in the said response, briefly that each of the groups is related, all claims, groups and species, can be examined without serious burden, that a search of tumor cell antibodies would provide useful information regarding other types of antibodies, such as antibodies to T cells.

Applicant's argument has been fully considered but is not persuasive.

There are two criteria for a proper requirement for restriction between patentably distinct inventions:

> (1) The inventions must be independent (see MPEP 802.01, 806.04, 808.01) or distinct as claimed (see MPEP 806.05 - 806.05(I)); and
>
> (2) There must be a serious burden on the Examiner if restriction is not required (see MPEP 803.02 806.04(a) - (j), 808.01(a) and 808.02).
>
> Regarding undue burden, the M.P.E.P. 803 (July 1998) states that: For purposes of the initial requirement, a serious burden on the examiner may be prima facie shown if the examiner shows by appropriate explanation either separate classification, separate status in the art, or a different field of search.

The restriction requirement enunciated in the previous Office Action meets this criterion of serious burden and therefore establishes that serious burden is placed on the Examiner by the examination of additional Groups. The inventions are distinct for reasons elaborated in paragraphs 2-5 of the previous Office Action. With regard to Applicant's argument pertaining to antibodies, antibodies to T cells are classified in Class 530, subclass 388.73, whereas antibodies to tumor cells are classified in Class 530, subclass 388.8, and tumor cells derive from almost any type of cell, not just T cell, and the tumor cell surface marker is not necessarily present on the non-malignant parental cell type, thus necessitating a separate classification, separate status in the art

and a different field of search. Applicant is reminded that if upon consideration of a search a species appears to be free of the prior art, the search will be extended to another species.

The requirement is still deemed proper and is therefore made FINAL.

Accordingly, claims 6-8, 10-15, 17 and 18 (non-elected species of Group I) and claims 20-60 (non-elected groups II-V) are withdrawn from further consideration by the Examiner, 37 CFR 1.142(b), as being drawn to non-elected inventions.

Claims 1-5, 9, 16 and 19 are currently being examined.

4. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP 602.01 and 602.02.

The oath or declaration is defective because:

The preliminary amendment filed 3/26/04 is not referred to in the declaration.

5. The amendment filed 3/26/04 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: the incorporation by reference of provisional application serial no. 60/457,896.

To obviate this objection, Applicant must submit a new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date and said oath or declaration must refer to the preliminary amendment filed 3/26/04.

6. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code on page 19 at the Table 1 legend. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP 608.01.

Appropriate correction is required

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-5, 9, 16 and 19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification does not provide adequate written description of the claimed invention. The legal standard for sufficiency of a patent's (or a specification's) written description is whether that description "reasonably conveys to the artisan that the inventor had possession at that time of the. . .claimed subject matter", Vas-Cath, Inc. V. Mahurkar, 19 USPQ2d 1111 (Fed. Cir. 1991). In the instant case, the specification does not convey to the artisan that the Applicant had possession at the time of invention of the claimed composition recited in the instant claims.

The instant claims encompass a composition that comprises fragments of an isolated MHC class I alpha 3 domain and/or a fragment of a β2m molecule and/or a fragment of an antibody specific for a cell surface marker, including those recited in the instant claims, said fragments not having functional activity, such as binding CD8 and/or β2m in the case of MHC class I alpha 3 domain fragments, β2m fragments that don't bind MHC class I molecules effectively or at all, and antibody fragments that do not bind antigen.

The instant specification discloses that an MHC class I alpha 3 domain fragment is identical to the sequence described by Fayen et al (1995), and that fragment that has substitutions of less than 1-20 amino acids which result in no more than a factor of 10 reduction in affinity for β2m or extends further into the transmembrane and/or the alpha 2 domain of the native alpha chain sequence and to which β2m binds with an affinity that remains less than one tenth the binding affinity of β2m for the intact MHC class I alpha chain or is shorter by any amount which is still compatible with no more than a factor of 10 reduction in affinity for β2m will be referred to as an MHC class I alpha 3 domain ([0017], [0040]). The specification further disclose that fragments of β2m that are useful in the invention would have to retain the ability to associate with the MHC class I alpha 3 domain, and preferably, retain the ability to associate with other domains of the intact alpha chain ([0042]). The specification discloses that the antibodies of the invention target the alpha 3 domain/β2m /peptide complexes to target cells ([0011], [0012]). The specification discloses antigen binding antibody fragments that are Fab, $F(ab')_2$, Fv and scFv ([0064], [0067]).

The specification does not disclose which substitutions or deletions are compatible with retaining functional activity of the alpha 3 domain fragments, nor of the β2m fragments, nor which antibody fragments bind antigen except for those antibody fragments that are Fab, $F(ab')_2$, Fv and scFv.

The instant disclosure does not adequately describe the scope of the claimed genus, which encompasses a substantial variety of subgenera of "fragments". Since the disclosure fails to provide sufficient relevant identifying characteristics, and because the genus is highly variant, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus as broadly claimed.

9. Claims 1-5, 9, 16 and 19 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

A. The incorporation of essential material in the specification by reference to a foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. See *In re Hawkins*, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); *In re Hawkins*, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and *In re Hawkins*, 486 F.2d 577, 179 USPQ 167 (CCPA 1973).

The attempt to incorporate subject matter into this application by reference to Fayen et al (Mol. Immunol. 32(4): 267-275, 1995) in the specification at [0017] is improper because essential matter can only be incoporated by reference to (1) a U.S. patent or (2) a pending U.S. application, subject to the conditions set forth below.

Essential material is defined as that which is necessary to (1) describe the claimed invention, (2) provide an enabling disclosure of the claimed invention, or (3) describe thebest mode (35 U.S.C. 112). In any application which is to issue as a U.S. patent, essentialmaterial may not be incorporated by reference to (1) patents or applications published by foreign countries or a regional patent office, (2) non-patent publications, (3) a U.S. patent or application which itself incorporates essential material by reference, or (4) a foreign application.

Essential material may not be incorporated by reference to non-patent publications, and the specification at [0017] refers to the fragment of complete human HLA-A*0201 alpha chain sequence taught by Fayen et al and disclosed substitutions thereto "will be referred to as an MHC class I α3 domain."

B. The specification does not disclose how to make and/or use the instant invention, a composition comprising one or more MHC class I alpha 3 domain fragments, and/or β2m fragments, and/or antibody fragments, with the exception of antibody fragments that are Fab, $F(ab')_2$, Fv and scFv.

The specification has not enabled the breadth of the claimed invention because the claims encompass a composition that comprises fragments of an isolated MHC class I alpha 3 domain and/or a fragment of a β2m molecule and/or a fragment of an antibody specific for a cell surface marker, including those recited in the instant claims, said fragments not having functional activity, such as binding CD8 and/or β2m in the case of MHC class I alpha 3 domain fragments, β2m fragments that don't bind MHC class I molecules effectively or at all, and antibody fragments that do not bind antigen. The state of the art is such that it is unpredictable in the absence of appropriate evidence whether the claimed compositions can be made and used.

The instant specification discloses that an MHC class I alpha 3 domain fragment is identical to the sequence described by Fayen et al (1995), and that fragment that has substitutions of less than 1-20 amino acids which result in no more than a factor of 10 reduction in affinity for β2m or extends further into the transmembrane and/or the alpha 2 domain of the native alpha chain sequence and to which β2m binds with an affinity that remains less than one tenth the binding affinity of β2m for the intact MHC class I alpha chain or is shorter by any amount which is still compatible with no more than a factor of 10 reduction in affinity for β2m will be referred to as an MHC class I alpha 3 domain ([0017], [0040]). The specification further disclose that fragments of β2m that are useful in the invention would have to retain the ability to associate with the MHC class I alpha 3 domain, and preferably, retain the ability to associate with other domains of the intact alpha chain ([0042]). The specification discloses that the antibodies of the invention target the alpha 3 domain/β2m /peptide complexes to target cells ([0011], [0012]). The specification discloses antigen binding antibody fragments that are Fab, $F(ab')_2$, Fv and scFv ([0064], [0067]).

The specification does not disclose which substitutions or deletions are compatible with retaining functional activity of the alpha 3 domain fragments, nor of the β2m fragments, nor which antibody fragments bind antigen except for those antibody fragments that are Fab, $F(ab')_2$, Fv and scFv.

Evidentiary reference Fayen et al (Mol. Immunol. 32(4): 267-275, 1995) teach that the alpha 3 domain can function as an independent structural unit to bind CD8α, but that interaction of the alpha 3 domain with β2m might impact affinity of binding of the alpha 3 domain with CD8α (especially Abstract and Discussion).

Evidentiary reference Whitman et al (Applicant's IDS reference) teach that the alpha 3 domain binds β2m and binds CD8αα with a dependence on the alpha 3 CD loop, and that a single amino acid mutation in the CD loop alters the direct binding of the alpha 3 domain to CD8αα. Whitman et al further teach that other mutations in the alpha 3 domain of class I MHC can also lead to changes in β2m binding (especially Abstract and sentence spanning pages 141 and 142).

There is insufficient guidance in the specification as to how to make and/or use instant invention. Undue experimentation would be required of one skilled in the art to practice the instant invention. See In re Wands 8 USPQ2d 1400 (CAFC 1988).

10. No claim is allowed.

11. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware of in the specification.

12. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Marianne DiBrino whose telephone number is 571-272-0842. The Examiner can normally be reached on Monday, Tuesday, Thursday and Friday.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Christina Y. Chan, can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Marianne DiBrino, Ph.D.
Patent Examiner /Group 1640/Technology Center 1600
May 26, 2005

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600